Applicant: Jean I. Montagu et al. Attorney's Docket No.: 13165-0005US1

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# Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

# Listing of Claims:

 (Currently Amended) An array reader suitable for clinical purposes for reading a two-dimensional array of features on a planar substrate, in which the features carry photoresponsive markers, the markers capable of emitting light upon excitation, the array reader comprising:

an illumination system for simultaneously exciting multiple photo-responsive markers distributed in a two-dimensional array over <u>a planar extent of</u> the substrate,

and an image collection and recording system having a field of view for emissions from the features on the substrate,

wherein:

the reader has no mechanism for moving the array relative to said systems during reading of the array,

the illumination system comprises a light source in the form of at least one light-emitting diode arranged to flood entirely the two-dimensional array with light at an excitation wavelength, along an illumination path disposed at an angle  $(\theta)$  between about 20° and 50° to the [[plane]] planar extent of the substrate,

the image collection and recording system\_having an image-acquiring axis substantially normal to the [[plane]] <u>planar extent</u> of the substrate carrying the array, employing a two-dimensional sensor comprising a solid-state array of photosensitive elements, and the image collection and recording system constructed and arranged to apply in a <u>single frame</u> an image of the <u>entire</u> array of features upon the solid-state array of size of the same order of magnitude as the size of the array of <u>features</u>, <u>e.g.-the size defined as being</u> within a range [[of]] <u>between</u> magnification of up to about 25% [[or]] <u>and</u> reduction down to 75%, the image collection and recording system having an intermediate numerical aperture NA of between NA=0.3 and

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NA=0.60 to enable recording the image of fluorescenee-from the excited two-dimensional array with clinical accuracy and without translation of the array.

(Cancelled)

 (Currently amended) The array reader of claim 1 in which the image collection and recording system has an effective aperture between NA=0.3 and NA=60 NA between about 4.0 and 5.5.

(Cancelled)

5. (Cancelled)

 (Currently Amended) The illumination system of claim 1 constructed and arranged to provide <u>from the at least one light-emitting diode</u>, excitation illumination over the entire two-dimensional array on the substrate of a power density greater than 30 mW/cm<sup>2</sup>.

(Cancelled)

 (Currently Amended) The array reader of claim 1 in which the field of view of the array reader has a diameter of the order of 10 mm or more.

9. (Cancelled)

(Cancelled)

 (Previously Presented) The array reader of claim 1 constructed and arranged to deliver to said solid state sensor array an image of the field of view reduced between about 30% and 50%. Applicant: Jean I. Montagu et al. Attorney's Docket No.: 13165-0005US1

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12-13. (Cancelled)

14-19 (Cancelled)

20. (Cancelled)

- 21. (Previously Presented) The array reader of claim 1 in combination with a substrate carrying excitation energy reference features distributed across said two-dimensional array of features, said image collection and recording system including a normalizing arrangement for normalizing data detected in the vicinity of respective reference features based on the quantity of detected emission from the respective reference features.
- 22 (Currently amended) The array reader of claim 1 in which said illumination system comprises at least two different light source sub-systems respectively of substantially different wavelengths, each associated with a respective optical system delivering light along a path, each light source sub-system comprising at least one light-emitting diode and being arranged to flood entirely the two dimensional array of features with light, the paths of said subsystems to said substrate lying along respectively different axes, the axes being spaced apart about said substrate.
  - 23. (Cancelled)
- 24 (Previously Presented) The array reader of claim 1 in which said illuminating system includes light source diodes selected respectively to excite Cy3 and Cy5, and said image collection and recording system includes changeable band-pass filters suitable to permit passage of emissions respectively from Cy3 and Cy5 or a single band-pass filter is provided suitable to permit multiple band-pass emissions of Cv3 and Cv5.

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26. (Currently Amended) The array reader of claim 1 in which said illumination system includes a diode light source followed by a homogenizer effective to reduce variation in flux density across the two dimensional field of illumination.

# 27-38. (Cancelled)

39. (Currently Amended) A method employing the array reader of claim 1 for detecting a physiological condition. A fluorescence reader-based diagnostic method-for-a disease for which there is a set of known protein biomarkers in blood or other body constituent, comprising the steps of (1) providing a two-dimensional array of different reagents on a planar extent of a substrate, the reagents respectively specific to bind members of a set of said biomarkers capable of determining the physiological condition diagnosing the disease, (2) exposing the array to fluorophore-labeled blood or body-constituent extract of an individual containing the biomarkers if present in the individual's blood or body constituent, (3) while the array is stationary, with said illumination system of the reader, exciting the array by simultaneously illuminating the entire two-dimensional array by light at fluorophore-excitation wavelength employing dark field illumination, (4) with the image collection and recording system of the reader, capturing a fluorescence image of the entire two-dimensional excited array on a single frame of-an imager comprising a solid-state array, and analyzing the fluorescence image for the presence of the physiological conditiondisease.

### (Cancelled)

41. (Currently Amended) The method of claim 39 in which fluorescence intensity reference features are distributed through the array and the detected radiation from said biomarkers is normalized by the reader based on the response of said reference[[s]] features to said illumination.

### 42-44. (Cancelled)

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45. (Currently Amended) A method <u>employing the array reader of claim 1</u> of reading an array on a substrate having features that include fluorophores, in which the array includes intensity calibration features of fluorescing character generally proportional in emission intensity to their illumination over the range of operable illumination intensities, including, forming an image of the array employing [[an]] <u>the array reader</u>, and normalizing recorded array data during the reading of the array [[from]] <u>based on emissions from</u> nearby intensity calibration features within the array.

#### 46-50 Cancelled

51. (New) The array reader of claim 1 in which the image collection and recording system has a field of view on the substrate of area between about 50 mm² and 300 mm².